UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/888,235	06/22/2001	Joan P. Blonder	42830-00234	8106

25231 7590 07/12/2006

MARSH, FISCHMANN & BREYFOGLE LLP
3151 SOUTH VAUGHN WAY
SUITE 411
AURORA, CO 80014

EXAMINER	
LI, BAO Q	

ART UNIT	PAPER NUMBER
1648	

DATE MAILED: 07/12/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

UNITED STATES PATENT AND TRADEMARK OFFICE

Commissioner for Patents
United States Patent and Trademark Office
P.O. Box 1450
Alexandria, VA 22313-1450
www.uspto.gov

BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

Application Number: 09/888,235
Filing Date: June 22, 2001
Appellant(s): BLONDER ET AL.

ROSS E. BREYFOGLE
For Appellant

EXAMINER'S ANSWER

This is in response to the appeal brief filed May 01, 2006 appealing from the Office action mailed June 27, 2005.

(1) Real Party in Interest

A statement identifying by name the real party in interest is contained in the brief.

(2) Related Appeals and Interferences

The examiner is not aware of any related appeals, interferences, or judicial proceedings, which will directly affect or be directly affected by or have a bearing on the Board's decision in the pending appeal.

(3) Status of Claims

The statement of the status of claims contained in the brief is incorrect. A correct statement of the status of the claims is as follows:

Claims 148-149 have been amended, and claims 150-197 have been canceled, which are submitted as a supplemental amendment filed and entered after the final rejection and before the current Appeal Brief on April 28, 2006.

This appeal involves claims 1, 4-7, 9-31, 33-37, 39-44 and 148-149.

(4) Status of Amendments After Final

The appellant's statement of the status of amendments after final rejection contained in the brief is correct.

The amendment filed after final rejection on April 28, 2006 has been entered.

(6) Grounds of Rejection to be reviewed on Appeal

The appellant's statement of the grounds of rejection to be reviewed on appeal is substantially correct.

Claims 1, 4-7, 9-31, 33-37, 39-44 and 148-149 are rejected under 35 U.S.C. 103(a) as being unpatentable over Alonso et al. (EP 0860 166A1) in view of Hale et al. (US patent No. 5, 607,691A) and Viegas et al. (a: US Patent No. 5,300,295A).

The following grounds of rejections are not presented for review on appeal because they have been withdrawn by the examiner:

A. Claims 1, 4-7, 9-31, 33-37, 39-44, 148-149 are rejected under 35 USC § 102 (b) for by Alonso et al. (EP 0860 166A1) in view of Hale et al. (US patent No. 5, 607,691A) and Viegas et al. (a: US Patent No. 5,300,295A).

B. Claims 1, 31, 33-44 and 148-149 are rejected under 35 USC § 112 1st paragraph.

(7) Claims Appendix

The copy of the appealed claims contained in the Appendix to the brief is correct.

(8) Evidence Relied Upon

Alonso et al. (EP 0860 166A1)

Hale et al. (US patent No. 5, 607,691A)

Viegas et al. (US Patent No. 5,300,295A).

(9) Grounds of Rejection

The following ground(s) of rejection are applicable to the appealed claims:

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1, 4-7, 9-31, 33-37, 39-44 and 148-149 are rejected under 35 U.S.C. 103(a) as being unpatentable over Alonso et al. (EP 0860 166A1) in view of Hale et al. (US patent No. 5, 607,691A) and Viegas et al. (a: US Patent No. 5,300,295A).

The claimed invention is directed to a composition comprising an antigen, an adjuvant, a polyoxalkylene block copolymer and aqueous liquid, wherein the copolymer in the composition exhibits a thermal reverse viscosity property within the temperature range from 1°C to 37°C. The composition comprises 60 to 85% weight of aqueous liquid, 0.0001 to 5% weigh of antigen, 5 to 33% weight of copolymer, and 0.01 to 10.0 % weight of adjuvant. The polyoxylkylene block copolymer comprises at least one block of a first and one block of a second polyoxyalkelen block

copolymer, wherein at least one block of the first copolymer is a polyoxyethylene (PEO) formulated as HO(C2H4O)b(C3H6O)a(C2H4O6)bH (a is between 15-80 and b is between 50-150), and at least one block of the second copolymer is polyoxypropylene (PPO) formulated as H(OCH2CH2)b[(OCHCH2)CH3]a(OCH2CH2)bOH (a is 20-80 and b is independent 15-60). The scope of the antigen is selected from an antigen selected from group consisting of antigen from bacteria, protozoa, fungus, hookworm, virus and combination thereof. The scope of an adjuvant can be selected from many adjuvants except alum. The composition can be in the form of dispense droplets in a mist spray produced by a nebulizer.

Alonso et al. teach an immunogenic composition and a method for making the same, wherein the immunogenic composition comprise an antigen, such as diphtheria toxoid, an adjuvant, i.e. chitosan, a polyoxyalkylene block copolymer such as PEO or PEO-PPO and water. Alonso et al. teach that the chitosan and other nonionic macromolecule, such as PEO-PPO forms nanoparticle in a non-extreme pH and non-organic solvent, wherein the proportions of chitosan and copolymer vary enormously according to the size of the nanoparticle. For example, the composition of the nanoparticles sizing with 685±27 nm comprises about 0.14% (w/w) of chitosan, 0.014% (w/w) of tetanus toxoid, 0.02% (w/w) sodium tripolyphosphate, 7% (w/w) of PEO-PPO (Because the ration of chitosan to PEO-PPO is 1:50, the polymer concentration is 0.014% x 50 = 7%) and make up water proportion is approximately 93% (w/w) [100-(7+0.14+0.114+0.02)] = 92.866% ≈ 93%). The Tables disclosed by Alonso et al. from which the examiner were used for calculating the proportions and supporting the rejection are listed in the following page.

Moreover, Alonso et al. teach that the antigen can be selected from any peptide, protein, polysaccharide or polynucleotide that exhibits an antigenic activity, and the total weight of the copolymer may vary from 0% to 60% (Claims 6-13).

Hence, the composition disclosed by Alonso et al. comprises substantially the same major ingredients as what they are drafted in the claims.

Example 1. The size, zeta potential and BSA association efficiency for this formulation are 402 nm, 46 mV and 100% respectively. (Please see page 4 of EP 0 860,166A1).

Chitosan base	0.14 %
Sodium tripolyphosphate	0.02 %
BSA	0.014%
Water	up to 100%

Example 3. Association of BSA to Chitosan/PEO-PPO (1:25) nanoparticles. The composition of the formulation in % (w/w) for size at 741 nm, zeta potential at 34 mV and BSA efficiency at 45.9% is as follows: (Please see the 1st Table on page 5 of EP 0 860 166A1)

Chitosan base	0.14 %
PEO-PPO	3.50 %
Sodium tripolyphosphate	0.02 %
BSA	0.014%
Water	up to 100%

Example 5. Nanoparticles are prepared as described in example 1 but adding diphtheria toxoid instead of BSA to the chitosan solution at the concentration indicated above. However, the ratio of the chitosan/PEO-PPO copolymer varies according to the size of the nanoparticle in the composition (Please see Table 1 on page 6 of EP 0 860 166A1).

Table 1

Mean values of particle size and zeta potential of nanoparticles composed of different chitosan/PEO-PPO ratios.		
Chitosan/PEO-PPO (w/w)	Size* (nm)	Zeta potential # (mV)
1/0	275 ± 17	44 ± 1
1/2.5	283 ± 11	41 ± 2
1/5	300 ± 14	40 ± 1
1/25	430 ± 20	28 ± 1
1/50	685 ± 27	18 ± 1

* Determined by Photon Correlation Spectroscopy
# Determined by Laser Doppler Anemometry

Therefore, the concentration of each components for the composition comprising nanoparticles at size of 685±27 nm would be calculated set forth in Table A below, wherein the ration of Chitosan to PEO-PPO is 1:50 (w/w)

Table A

Chitosan	0.14%
Antigen (diphtheria toxoid)	0.014%
Sodium tripolyphosphate	0.02%
PEO-PPO (1:50)	7%
Water	up to 100

The concentrations of each ingredient in the claimed composition are shown in Table B below:

Table B

Adjuvant	0.01 to 10.0 % (w/w)
Antigen	0.0001 to 5 % (w/w)
PEO-PPO polymer	5 to 33 % (w/w)
Aqueous liquid (PBS-Buffered saline)	60 to 85 % (w/w)

It should be noted that the current application teaches that chitosan is used in the example in the specification and claimed as an adjuvant, diphtheria toxoid is claimed as an antigen. The composition is prepared with phosphate buffer saline (PBS). Pluronic® F127 * is used a PEO-PPO block copolymer * Pluronic® F127 is poly(ethylene oxide)-poly(propylene oxide)-poly(ethylene oxide) PEO-PPO-PEO block copolymer. Please see pages 26-27 of specification of current application and claims)

Alonso et al. do not explicitly teach the general structure and reverse thermal sensitivity of said PEO-PPO block copolymer.

Viegas et al. teach a therapeutic composition comprising a reverse thermal sensitive block copolymer, wherein said block copolymer is selected from wide variety of polyoxyalkelene copolymers (PEO-PPO) that exhibit a reverse thermal viscosity characteristics, i.e. being a low viscosity liquid at the ambient temperature (37°C), but forms a semisolid gel at mammalian body temperatures (See column 2). The preferred polyxyalkelene block copolymers

can be selected from several block polymers including $HO(C_2H_4O)_b(C_3H_6O)_a(C_3H_6O)_bH$ (formula "IV") and formula of $H(OC_2H_2CH_2)_b[(OCHCH_2)CH_3]_a(OC_2H_2CH_2)_bOH$, (formula "VI") (See column 6). Viegas et al. further teach that in formula "VI", the integer "a" is taught as 67, which is within the limitation of the claimed integer of "a" as 20 to 80, and the integer "b" as 49, which meets the limitations of the claims 11-14 (See columns 5-6 and column 13).

Viegas et al. further teach that such kind of polyoxalkylen copolymer, for example. Pluronic® F127, is suitable for preparing a pharmaceutical composition that exhibits the reverse thermal viscosity property, wherein the concentration of said polyoxalkylen block copolymer vary greatly from 2 % to 50% or even higher (See columns 9-13).

Hence, PEO-PPO block copolymer has already been proved to be a thermal sensitive copolymer and useful for formulating as a pharmaceutical composition evidenced by Viagas et al., The proportions of the essential active components comprised in the composition disclosed by Alonso et al. are all within the same range as what they are claimed. The disclosure by Alonso et al. in view of the Viagas et al. teach the composition having substantial same limitations of the claims or at least an obvious modification of the composition cited in the claims.

The only minor difference between the claims and the composition disclosed by Alonso et al. is the 7~8% more water than that of the claims. Regarding this, Appellants' attentions are directed to the MPEP, which cites: ***Generally, differences in concentration or temperature will not support the patentability of subject matter encompassed by the prior art unless there is evidence indicating such concentration or temperature is critical. "[W]here the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation."*** *In re Aller.*

Therefore, without indicating how critical this 7 to 8% water makes the claimed composition distinct from the composition disclosed by the prior art, a modification of such inert element in a composition would have been obvious for any ordinary skill in the art since it is able to get a similar biological effect compared with that non-modified composition absence any unexpected result to the contrary.

Therefore, it is conclude that "***It is not inventive to discover the optimum or workable ranges by routine experimentation. Generally, differences in concentration or temperature will***

not support the patentability of subject matter encompassed by the prior art unless there is evidence indicating such concentration or temperature is critical. "

Alonso et al. do not teach to deliver a composition as a droplet or mist produced by a nebulizer, preferably a nasal nebulizer.

Hale et al. teaches that a pharmaceutical composition comprising a biological protein or peptide molecule can be formulated with some synthetic polymers, such as polyethylenes copolymers (See lines 45-67 in column 47 and Table 2), so that it can be suitably delivered as topic aerosol spray with high permeability through dermal or mucosa, and it is capable of being inhaled into the bronchioles or nasal passages. Specially, the composition can be packaged in metered dose inhaler or nebulizer or in a mist sprayer to be produced as an aerosol includes a gas-born suspension of droplets of the compounds (See lines 10-20 on column 53).

Therefore, in order to make an immunogenic composition with more biocompatibilities, it would have been obvious for a person of ordinary skill in the art to make an immunogenic composition taught by Alonso et al. with a reverse thermal viscosity property by using the PEO-PPO copolymer taught by Viegas et al. and adapting the method taught by Hale et al. Hereby, the composition can be applied with more flexible pharmaceutical delivery formulations as taught by Hale et al. for producing more efficient and direct immune response when it is used as a regional immunological therapeutic agent.

As there are no unexpected results have been provided, hence the claimed invention as a whole is prima facie obvious absence unexpected results.

(10) Response to Argument.

Appellants argue that the rejection of claims 1, 4-7, 9-37, 39-44 and 148-149 under *35 USC § 103* is not proper because the composition taught by Alonso et al. is a drug delivery nanoparticles, which does not contain 60 to 85% (wt/wt) aqueous liquid and 5 to 33% (wt/wt) polyoxykallene block copolymer. Moreover, Alonso et al. do not teach that the copolymer exhibits a reverse thermal viscosity behavior as required in appealed claim 1.

Appellants further argue that the secondary references Viegas et al. and Hall do not make up for the deficiencies of Alonso et al. to render the claimed subject matter obvious under - ***35 USC § 103.***

Regarding the primary reference by Alonso et al. Appellants submit the following arguments:

A. The disclosure by Alonso et al. is directed to a drug delivery nanoparticle, which has different manufacture process for making and different purpose of using a product then the claimed invention.

B. The examiner's characterization of Alonso et al. confuses teachings by Alonso et al. In particular, appellants assert that they cannot find the combination of constituents asserted by the examiner, i.e. the composition with the nanoparticle sizing with 685 ±27 nm comprising about 0.14% (w/w) of chitosan, 0.014% of tetanus toxoid, 0.02% (w/w) sodium triphosphate, 7% (w/w) of PEO-PPO and 93% (w/w) water.

C. The drug delivery nanoparticles disclosed by Alonso et al. do not contain the combination of components recited in appealed claim 1.

D. The formulation medium disclosed by Alonso et al. does not contain the combination of components recited in appealed claim 1, which include:

1. The formulation medium for making nanoparticles contains from 60 weight percent to 85 weight percent aqueous liquid;

2. The formulation medium for making nanoparticles contains 5 weight percent to 33 weight percent polyoxyalkylene block copolymer.

3. the formation medium for making nanoparticles contains either 93% water or 7% PEO-PPO as asserted by the examiner.

4. Alonso et al. do not disclose, expressly or inherently, any composition that has reverse thermal viscosity behavior, such that the viscosity of the composition increase over some temperature range within 1 °C to 37°C.

In response to appellants' argument regarding the calculation of composition comprising the nanoparticle sizing with 685 ±27 nm, appellants' attentions are directed to the disclosures of the Tables and citations by Alonso et al. on pages 4-6 set forth below:

Alonso et al. teach in Example 3 that Association of BSA to Chitosan/PEO-PPO (1:25) nanoparticles. The composition of the formulation in % (w/w) for size at 741 nm, zeta potential

at 34 mV and BSA efficiency at 45.9% was as follows: (Please see the 1st Table on page 5 of EP 0 860 166A1)

Chitosan base	0.14 %
PEO-PPO	3.50 %
Sodium tripolyphosphate	0.02 %
BSA	0.014%
Water	up to 100%

Alonso et al. teach in Example 5. that nanoparticles are prepared as described in example 1 but adding diphtheria toxoid instead of BSA to the chitosan solution at the concentration indicated above. However, the ratio of the chitosan to PEO-PPO copolymer varies based on the size of the nanoparticle accordingly (Please see Table 1 on page 6 of EP 0 860 166A1).

Table 1

Mean values of particle size and zeta potential of nanoparticles composed of different chitosan/PEO-PPO ratios.		
Chitosan/PEO-PPO (w/w)	Size* (nm)	Zeta potential # (mV)
1/0	275 ± 17	44 ± 1
1/2.5	283 ± 11	41 ± 2
1/5	300 ± 14	40 ± 1
1/25	430 ± 20	28 ± 1
1/50	685 ± 27	18 ± 1

* Determined by Photon Correlation Spectroscopy
# Determined by Laser Doppler Anemometry

Therefore, the concentrations of each component for the composition comprising nanoparticles at size 685±27 nm would be calculated in Table A below, in which the ration of Chitosan to PEO-PPO is 1:50 (w/w)

Chitosan	0.14%
Antigen (dipherial toxoid)	0.014%
Sodium tripolyphosphate	0.02%
PEO-PPO (1:50)	7% (50 x 0.14%)
Water	up to 100 [100-(7+0.02+0.14=0.014)]

Furthermore, Alonso et al. teaches and suggests that the immunogenic composition can be prepared with variety of antigens materials selected from peptide, protein, oligonucleotide, RNA, DNA etc.

To this context, the ingredients and proportions of each ingredient in both compositions by Alonso et al. and in claims are substantially same, or at least an obvious version with a minor modification (Please see Table below).

Table A (Alonso et al.) Table B (Claims)

Chitosan	0.14%	Adjuvant	0.01 to 10.0 % (w/w)
Antigen (diphtheria toxoid)	0.014%	Antigen	0.0001 to 5 % (w/w)
PEO-PPO	7%	PEO-PPO polymer	5 to 33 %) w/w)
Water	~92.87%	Aqueous liquide	60 to 85 % (w/w)
Sodium tripolyphosphate	0.02%		

In the instant case, the specification discloses to use PBS as non-organic solvent to dissolve the PEO-PPO and other components. The PBS is a NaCl in Na2HPO4/NaH2PO4 buffer saline with a neutral pH around 7.2.

Therefore, regardless whether the chitosan with copolymer forms a nanoparticle or not, the composition, especially the nanoparticle having a size at 685±27 nm comprises the same active ingredients and at least the major immunological and pharmaceutical active components are in the same ranges as what they been claimed in the current application.

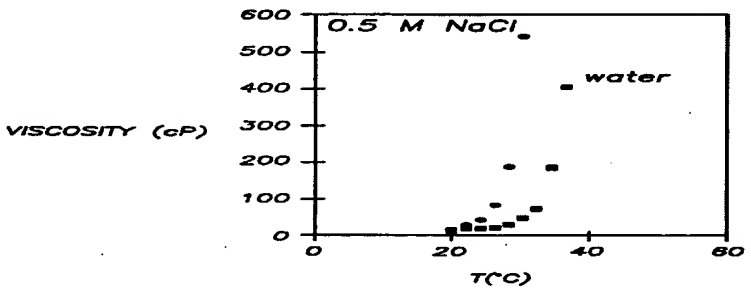
Regarding the minor proportional difference of 7-8% water in said defined functional composition, MPEP cites: ***Generally, differences in concentration or temperature will not support the patentability of subject matter encompassed by the prior art unless there is evidence indicating such concentration or temperature is critical. "[W]here the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation."*** *In re Aller, 220 F.2d 454, 456, 105 USPQ 233, 235 (CCPA 1955).*

Because the active components in the immunological compositions disclosed by Alonso et al. comprise an antigen, an adjuvant and a copolymer (PEO-PPO), which are same to the claimed composition, the 7% water without any specified biological or immunological function, would have been considered as an inert element, and such miner difference would also have been considered as an obvious modification because it would not influence the immunological and therapeutic function of said composition.

To support this notion that a 7 % water difference will not influence the reverse heat sensitivity property of a PEO-PPO block copolymer in a composition. Viegas et al. teach that the wide varieties of polyoxalkylene copolymers in considerable large ranges of concentrations are suitable for preparing a pharmaceutical compositions that still exhibit such reverse heat sensitive property, such as from 1.0% to 10.0% or 10% to 50% etc (Claims 1-23 and columns 4 & 5).

In fact, this property is well known in the art that is substantiated by the evidenced provided by appellants in the IDS, which was submitted before the current Appeal Brief on April 11 2006. For example, the reference (WO 9700275) in said IDS teaches that a polymer PEO-PPO network in variety of concentrations exhibits of reversible thermal sensitive gelation characteristics. Any pharmaceutical composition comprising 0.01 to 20% (wt) or even more higher concentration of said PEO-PPO maintains the same reverse thermal sensitivity property in response to the temperature change from 0°C to about 37°C (See Fig. 12 and claims 1-74).

FIG. 12



(Fig. 2. A plot of viscosity vs. temperature for composition comprising 2.5wt % Pluronic ® F 127/polycarylic acid (1:10) prepared in (a) deionized water and (b) 0.5M NaCl solution.)

In the current situation, the proportions of the claimed copolymer vary from 5 to 33%, and the concentration of the PEO-PPO in the composition disclosed by Alonso et al. is 7 %.

They are in the range that the PEO-PPO is able to exhibit the reverse thermal viscosity property. To this context, the 7 % of water difference would not make the PEO-PPO loss its reverse heat sensitivity properties.

Because the chemical/physical characteristic and biological function of said PEO-PPO block copolymer would not have been changed by such 7 to 8% water miner modification, it would be concluded that "***It is not inventive to discover the optimum or workable ranges by routine experimentation. Generally, differences in concentration or temperature will not support the patentability of subject matter encompassed by the prior art unless there is evidence indicating such concentration or temperature is critical.*** " As there are no unexpected results have been provided, hence the claimed invention as a whole is prima facie obvious absence unexpected results.

While appellants admit that the Alonso et al disclose an immunogenic composition comprising chitosan, PEO-PPO copolymer and antigen or other therapeutic macromolecule (peptide, protein, oligonucleotide, RNA or DNA) prepared in a sodium triphosphate buffer saline they still argue that the disclosure by Alonso et al. is directed to a drug delivery nanoparticle, which has different manufacture process for making and different purpose of using a product then the claimed invention.

Regarding the argument of the process of making and using the product in the claims that is different from the prior art, MPEP in chapter 2100 cites: Even though product-by process claims are limited by and defined by the process, determination of patentability is based on the product itself. The patentability of a product does not depend on its method of production. If the product in the product-by -process claim is the same as, or obvious from a product in the prior art, the claim is unpatentable even though the prior product was made by a different process (See MPEP 2113).

In the instant case, the determination of the patentability or distinctiveness of the claimed composition is based product itself. By comparison from the tables shown in A & B, the active ingredients of the compositions disclosed by the prior art and in claims are substantially same or are considered to be an obvious modification for an ordinary skill in the art as discussed above.

Appellants are also reminded that the intended use cannot be weighted for determining patentability of a composition. Nevertheless, the utilities of bots compositions disclosed by the

cited prior art of Alonso et al. and claims are same because they are all drawn to an immunogenic composition for inducing an immune response.

It is also worthwhile to note, and Appellants cites in the Appeal Brief as well: "Alonso et al. teach that "The formation of nanoparticles occurs spontaneously due to the simultaneous precipitation of chitosan and the bioactive macromolecule caused by the incorporation of a molecule with a basic character, i.e. sodium triphosphate. This process can be also considered as a process of ionic gelation or ionic cross linking of chitosan with the counter anion. In this method, the utilization of organic solvents, extreme pH conditions or auxiliary substances of toxic nature are avoided." (Alonso et al. at page 2, lines 23-27).

In the instant case, a broad reasonable interpretation of the "aqueous liquid" cited in the claim can be any liquid solution rather than pure deionized water. Especially, according to the specification of current application, the immunogenic composition comprising chitosan and PEO-PPO block copolymer is prepared with a sodium phosphate buffer saline (NaCl in Na2HPO4/NaH2PO4 buffer saline with a neutral pH around 7.2). Therefore, such liquid solution is able to provide the positive charge from Na+ in solution for the chitosan and PEO-PPO copolymer presented in the claimed composition. To this context, the claimed product is still considered as a non-patently distinct product with an obvious modification of an inert element of 7~8% water for an ordinary skill in the art

Appellants further argue that the second references by Viegas et al. and Hall et al. do not make up for the deficiencies of Alonso et al. to render the claimed subject matter obvious under *35 USC § 103.*

In current condition, the primary reference by Alonso et al. teaches the main structural and immunological features of the claimed composition, i.e. a composition comprising an antigen, PEO-PPO copolymer, and a non-alum adjuvant and water. The reference of Viegas et al. reinforces the rejection because Viagas et al. teach that the PEO-PPO polymer is same copolymer disclosed by the primary reference of Alonso et al. which has a same structure and chemical/physical reverse thermal sensitivity property taught by Viagas et al.

For example, Viegas et al. teach a therapeutic composition comprising the reverse thermal sensitive block copolymer, wherein the block copolymer can be selected from wide variety of polyoxyalkelene copolymers (PEO-PPO), The preferred polyxyalkelene block

copolymers can be selected from several block polymers such as $HO(C_2H_4O)_b(C_3H_6O)_a(C_3H_6O)_bH$ (formula "IV") and formula of $H(OC_2H_2CH_2)_b[(OCHCH_2)CH_3]_a(OC_2H_2CH_2)_bOH$, (formula "VI") (See column 6). Viegas et al. further teach that for the formula "VI", the integer "a" is taught as 67, which is within the limitation of the claimed integer of "a" as 20 to 80, and the integer "b" is 49, which meets the limitations of the claims 11-14 (See columns 5-6 and column 13).

Viegas et al. further teach that wide rages of concentrations of said polyoxalkylen copolymers are suitable for preparing said pharmaceutical compositions with said reverse thermal viscosity property, wherein the proportion of said polyoxalkylen block copolymer vary from 10 to 50% or 10 to 40% or 20 to 80% depended on its molecular structure (formula) in the pharmaceutical composition (See lines 5-10 on column 13).

Viegas et al. further teach that the wide varieties of polyoxalkylene copolymers are suitable for the preparation of the pharmaceutical compositions, wherein the composition comprising said polyoxyalkylen block copolymers also having the reverse heat sensitive characteristics is in liquid form at ambient temperatures (37°C) and in gel form with a desired osmolality at mammalian body temperature (Claims 1-23 and columns 1 & 2).

Hence, it is still concluded that the disclosure of Alonso et al. in view of the Viegas et al. teach a composition having substantial same limitations or at least being an obvious version of the composition cited in the claims. In other ward, the claimed inventions is an obvious modification for an ordinary skill in the art absence unexpected result to the contrary.

Regarding the argument about Hale's reference, appellants are reminded that Hale et al. teach several choices for making a composition suitably for being delivered through dermal or skin or mucosal as aerosol spray mist produced by nebulizer. Hale et al. teach that such composition can be prepared by formulating a composition comprising a biological active molecule, such as protein, peptide, cytokine, hormone etc. with a synthetic copolymer, Regarding motivation, Hale et al. explicitly teach that the problem challenging the preparation of a therapeutic composition comprising a protein and peptide drug is associated with a conventional delivery strategy. Oral administration of these drugs is generally impractical due to degeneration and non-absorption in the gastrointestinal tract (Column 14). Therefore, in order to increase the biocompatibility of such therapeutic agent, Hale et al. teach that a pharmaceutical

composition comprising said therapeutic agent can be formulated with a synthetic copolymer, such that is can be more permeability through a nasal and/or pulmonary membranes, typically through an aerosol delivery, such as an inhaler or a nebulizer or in a mist sprayer (see lines 45-55 on col. 47 and column 53, lines 12-25 and Table 2 on col. 15-16). Hale et al. also teach that the synthetic copolymers can be polyethylene copolymers (See lines 45-67 in column 47).

Therefore, it would have been obvious for a person of ordinary skill in the art, in order to make an immunogenic composition having more biocompatible properties, to be motivated to prepare an immunogenic composition comprising an antigen, an adjuvant and PEO-PPO block copolymers with an inherent thermal sensitive characteristic, such that the immunogenic composition can be made with more biocompatible applications that are capable of being applied in more flexible physical and biological conditions, such as a liquid spray in room temperature and used as a gel form upon it needs to be applied onto a regional area through skin or mucus etc. for producing more direct and enhanced local immune response. Hence the claimed invention as a whole is prima facie obvious absence unexpected results.

(11) Related Proceeding(s) Appendix

No decision rendered by a court or the Board is identified by the examiner in the Related Appeals and Interferences section of this examiner's answer.

For the above reasons, it is believed that the rejections should be sustained.

Respectfully submitted,

Bao Qun Li

Conferees: Baoqun Li

Bruce Campell, SPE of Art Unit 1648

Brenda Brumback, SPE of Art Unit 1647

Bruce Campell

BRUCE R. CAMPELL, PH.D
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600

Brenda Brumback

BRENDA BRUMBACK
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600